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|---|--|---|
| FORM PTO-1390<br><br>U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE  |  | ATTORNEY DOCKET NUMBER<br><b>CELI-0296</b>                          |
| <b>TRANSMITTAL LETTER TO THE UNITED STATES<br/>         DESIGNATED/ELECTED OFFICE (DO/EO/US)<br/>         CONCERNING A FILING UNDER 35 U.S.C. 371</b>   |  | U.S. APPLICATION NO. (if known see 37 CFR 1.5)<br><b>10/533,003</b> |
| INTERNATIONAL APPLICATION NO.<br><b>PCT/GB2003/004639</b>   | INTERNATIONAL FILING DATE<br><b>28 October 2003 (28.10.2003)</b>   | PRIORITY DATE CLAIMED<br><b>30 October 2002 (30.10.2002)</b>        |
| <b>TITLE OF INVENTION CHIMERIC CYTOPLASMIC SIGNALLING MOLECULES</b>   |  |   |
| <b>APPLICANT(S) FOR DO/EO/US Helene Margaret FINNEY and Alastair David Griffiths LAWSON</b>   |  |   |
| Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:   |  |   |
| 1. <input type="checkbox"/><br>2. <input checked="" type="checkbox"/><br>3. <input type="checkbox"/><br>4. <input type="checkbox"/><br>5. <input type="checkbox"/><br>6. <input type="checkbox"/><br>7. <input type="checkbox"/><br>8. <input type="checkbox"/><br>9. <input type="checkbox"/><br>10. <input type="checkbox"/>          | This is a <b>FIRST</b> submission of items concerning a filing under 35 U.S.C. 371.<br>This is a <b>SECOND</b> or <b>SUBSEQUENT</b> submission of items concerning a filing under 35 U.S.C. 371.<br>This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9), and (21) indicated below.<br>The US has been elected (Article 31).<br>A copy of the International Application as filed (35 U.S.C. 371(c)(2)).<br>a. <input type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau).<br>b. <input type="checkbox"/> has been communicated by the International Bureau.<br>c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US).<br>An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).<br>a. <input type="checkbox"/> is attached hereto.<br>b. <input type="checkbox"/> has been previously submitted under 35 U.S.C. 154(d)(4).<br>Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)).<br>a. <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau).<br>b. <input type="checkbox"/> have been communicated by the International Bureau.<br>c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired.<br>d. <input type="checkbox"/> have not been made and will not be made.<br>An English translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).<br>An oath or declaration of the inventor(s) 35 U.S.C. 371(c)(4).<br>An English translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)). |   |
| <b>Items 11. to 20. below concern other document(s) or information included:</b>  |  |   |
| 11. <input type="checkbox"/><br>12. <input type="checkbox"/><br>13. <input type="checkbox"/><br>14. <input type="checkbox"/><br>15. <input type="checkbox"/><br>16. <input type="checkbox"/><br>17. <input type="checkbox"/><br>18. <input type="checkbox"/><br>19. <input type="checkbox"/><br>20. <input checked="" type="checkbox"/> | An Information Disclosure Statement under 37 CFR 1.97 and 1.98.<br>An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.<br>A preliminary amendment.<br>An Application Data Sheet under 37 CFR 1.76.<br>A substitute specification.<br>A power of attorney and/or change of address letter.<br>A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 37 CFR 1.182-1.825.<br>A second copy of the published international application under 35 U.S.C. 154(d)(4).<br>A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).<br>Other items or information:<br>- <b>Response to Notification of Insufficient Fees;</b><br>- <b>a copy of the previously filed Preliminary Amendment;</b><br>- <b>a copy of the Notification of Insufficient Fees dated October 20, 2005;</b><br>- <b>a return postcard.</b>   |   |
| EXPRESS MAIL Mailing Label No. 482611909 US<br>Date of Deposit: December 16, 2005   |  |   |

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid IMB control number.

|  |              |   |                |  |    |
|--|--------------|---|----------------|--|----|
| U.S. APPLICATION NO. (if known 37 C.F.R. 1.5)<br><b>10/533,003</b>   |              | INTERNATIONAL APPLICATION NO.<br><b>PCT/GB03/04639</b>                        |                | ATTORNEY DOCKET NUMBER<br><b>CELL-0296</b> |    |
| The following fees are submitted:  |              |   |                |  |    |
| 21. <input type="checkbox"/> Basic national fee (37 CFR 1.492(a))  |              | <b>\$300</b>  |                | \$   |    |
| 22. <input type="checkbox"/> Examination fee (37 CFR 1.492(c))   |              |   |                | \$   |    |
| If written opinion prepared by ISA/US or the international preliminary examination report prepared by IPEA/US indicates all claims satisfy provisions of PCT Article 33(1)-(4)   |              | <b>\$0.00</b>   |                | \$   |    |
| All other situations   |              | <b>\$200</b>  |                |  |    |
| 23. <input type="checkbox"/> Search fee (37 CFR 1.492(b))  |              |   |                | \$   |    |
| If the written opinion of the ISA/US or the International preliminary examination report prepared by IPEA/US indicates all claims satisfy provisions of PCT Article 33(1)-(4)  |              | <b>\$0</b>  |                |  |    |
| Search fee (37 CFR 1.445(a)(2)) has been paid on the international application to the USPTO as an International Searching Authority  |              | <b>\$100</b>  |                |  |    |
| International Search Report prepared by an ISA other than the US and provided to the Office or previously communicated to the US by the IB   |              | <b>\$400</b>  |                |  |    |
| All other situations   |              | <b>\$500</b>  |                |  |    |
| <b>TOTAL of 21, 22 and 23 =</b>  |              |   |                | \$   |    |
| <input type="checkbox"/> Additional fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing in compliance with 37 CFR 1.821(c) or (e) or computer program listing filed in electronic medium) (37 CFR 1.492(j)). The fee is <b>\$250</b> for each additional 50 sheets of paper or fraction thereof. |              |   |                |  |    |
| Total Sheets   | Extra Sheets | Number of each additional 50 or fraction thereof (round up to a whole number) | RATE           |  |    |
| - 100 =  | /50=         |   | <b>X \$250</b> | \$   |    |
| Surcharge of <b>\$130.00</b> for furnishing any of the search fee, or the oath or declaration after the date of commencement of the national stage (37 CFR 1.492(h)).  |              |   |                | \$   |    |
| Claims   | Number Filed | Number Extra  | Rate           |  |    |
| Total claims   | - 20 =       |   | <b>X \$50</b>  | \$   |    |
| Independent Claims   | - 3 =        |   | <b>X \$200</b> | \$   |    |
| Multiple dependent claims(s) (if applicable)   |              |   | <b>+ \$360</b> | \$   |    |
| <b>TOTAL OF ABOVE CALCULATIONS =</b>   |              |   |                | \$   |    |
| <input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2.   |              |   |                | \$   |    |
| <b>SUBTOTAL =</b>  |              |   |                | \$   |    |
| Processing fee of <b>\$130.00</b> for furnishing the English translation later than 30 months from the earliest claimed priority date (37 CFR 1.492(i)).   |              |   |                | \$   |    |
| <b>TOTAL NATIONAL FEE =</b>  |              |   |                | \$   |    |
| Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). <b>\$40.00</b> per property +  |              |   |                |  |    |
| <b>TOTAL FEES ENCLOSED =</b>   |              |   |                | \$   |    |
|  |              |   |                | Amount to be: refunded                     | \$ |
|  |              |   |                | Amount to be charged                       | \$ |

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid LMB control number.

- a. ☐ A check in the amount of \$ \_\_\_\_\_ to cover the above fee is enclosed.
- b. ☐ Please charge my Deposit Account No. 23-3050 in the amount of \$ \_\_\_\_\_ to cover the above fees. A duplicate copy of this sheet is enclosed.
- c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 23-3050. A duplicate copy of this sheet is enclosed.

**NOTE:** Where an appropriate time limit under 37 CFR 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

**David A. Cherry**  
Woodcock Washburn LLP  
One Liberty Place - 46th Floor  
Philadelphia, PA 19103  
(215) 568-3100

SIGNATURE

**David A. Cherry**

NAME

**35,099**

REGISTRATION NUMBER

DOCKET NO.: CELL-0296

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of: **Helene Margaret FINNEY and Alastair David Griffiths**  
**LAWSON** Confirmation No.: 1691

U.S. Serial No.: 10/533,003

Group Art Unit: not yet assigned

U.S. Filing Date: April 28, 2005

Examiner: not yet assigned

For: **CHIMERIC CYTOPLASMIC SIGNALLING MOLECULES**

EXPRESS MAIL LABEL NO: EV 482611909 US  
DATE OF DEPOSIT: December 16, 2005

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

**RESPONSE TO NOTIFICATION OF INSUFFICIENT FEES**

In response to the "Notification of Insufficient Fees", dated October 20, 2005, applicant submits herewith, a copy of such notice. A Preliminary Amendment was filed in the U.S. Patent Office on October 18, 2005 removing improper multiple dependencies. The total number of claims for this application is 20, with 2 independent claims. Therefore, no additional claims fees are due at this time. A copy of the previously filed Preliminary Amendment is enclosed.

If it is determined that this is not correct, the Commissioner is hereby authorized to charge any additional fees to Deposit Account No. 23-3050.

Respectfully submitted,

Date: December 16, 2005

David A. Cherry  
Registration No. 35,099

WOODCOCK WASHBURN LLP  
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Telephone: (215) 568-3100

DOCKET NO.: CELL-0296  
Application No.: 10/533,003  
Preliminary Amendment - First Action Not Yet Received

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:  
Finney, H.M., et al.

Confirmation No.: Not yet assigned

Application No.: 10/533,003

Group Art Unit: Not yet assigned

International Serial No.:  
PCT/GB2003/004639

International Filing Date: October 28,  
2003

Filing Date: Herewith

Examiner: Not yet assigned

For: Chimeric Cytoplasmic Signalling Molecules

EXPRESS MAIL LABEL NO: EV 482612351 US  
DATE OF DEPOSIT: October 20, 2005

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

PRELIMINARY AMENDMENT PURSUANT TO 37 CFR § 1.115

Preliminary to examination of the above-captioned patent application, please amend the application as follows:

- ☐ Amendments to the Specification begin on page      of this paper.
- ☒ Amendments to the Claims are reflected in the listing of the claims which begins on page 2 of this paper.
- ☐ Amendments to the Drawings begin on page      of this paper and include an attached replacement sheet.
- ☒ Remarks begin on page 6 of this paper.

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

1. (currently amended) A nucleic acid molecule comprising a sequence encoding a cytoplasmic signalling molecule ~~comprising that comprises~~ at least two cytoplasmic signalling sequences, wherein at least one of the cytoplasmic signalling sequence sequences is derived from CD134 or ICOS the human inducible co-stimulator.
2. (currently amended) A nucleic acid molecule according to claim 1, wherein at least one of the cytoplasmic signalling sequence sequences is a primary cytoplasmic signalling sequence.
- 3-5. (canceled)
6. (currently amended) A nucleic acid molecule according to claim 1, wherein at least one of the cytoplasmic signalling sequence sequences is a secondary cytoplasmic signalling sequence.
7. (canceled)
8. (currently amended). A nucleic acid molecule according to ~~any one of claims 2 to 7~~ claim 2, which encodes comprising a sequence encoding a cytoplasmic signaling molecule that comprises three cytoplasmic signalling sequences.
9. (currently amended) A nucleic acid molecule according to ~~any one of claims 2 to 7~~ claim 2, wherein the first cytoplasmic signalling sequence encoded ~~for~~ in a reading frame is derived from CD134 or ICOS the human inducible co-stimulator.
10. (currently amended) A nucleic acid molecule according to claim 9, which encodes i) a cytoplasmic signalling sequence derived from CD134 followed in a reading frame by ii) a cytoplasmic signalling sequence derived from TCR $\zeta$ .

11. (currently amended) A nucleic acid molecule according to claim 9, which encodes i) a cytoplasmic signalling sequence derived from ICOS the human inducible co-stimulator followed in a reading frame by ii) a cytoplasmic signalling sequence derived from TCR $\zeta$ .

12. (currently amended) A nucleic acid molecule according to ~~any one of claims 2 to 7~~ claim 2, wherein the second cytoplasmic signalling sequence encoded ~~for~~ in a reading frame is derived from CD134 or ICOS the human inducible co-stimulator.

13-15. (canceled)

16. (currently amended) A nucleic acid molecule according to ~~claim 15~~ claim 8 which encodes in a reading frame i) a cytoplasmic signalling sequence derived from CD28, ii) a cytoplasmic signalling domain derived from TCR $\zeta$ , and iii) a cytoplasmic signalling sequence derived from CD134.

17. (currently amended) A nucleic acid molecule according to ~~claim 15~~ claim 8 which encodes in a reading frame i) a cytoplasmic signalling sequence derived from CD28, ii) a cytoplasmic signalling domain derived from TCR $\zeta$ , and iii) a cytoplasmic signalling sequence derived from ICOS the human inducible co-stimulator.

18. (currently amended) A nucleic acid molecule encoding a chimeric receptor protein, which comprises an extracellular ligand-binding domain, a transmembrane domain and a cytoplasmic signalling domain, wherein the cytoplasmic signalling domain is encoded by a nucleic acid sequence according to ~~any one of claims 1 to 17~~ claim 1.

19. (currently amended) A nucleic acid molecule encoding a chimeric receptor protein, which comprises an extracellular ligand-binding domain, a transmembrane domain and a cytoplasmic signalling domain, wherein the cytoplasmic signalling domain comprises a single cytoplasmic signalling sequence derived from CD134 or the human inducible co-stimulator.

20. (canceled)

21. (currently amended) A nucleic acid molecule according to ~~claims 18 and 20~~ claim 18 wherein the extracellular ligand-binding domain is an antibody, or an antigen-binding fragment thereof.

22-24. (canceled)

25. (currently amended) A vector comprising a nucleic acid molecule according to ~~any one of the preceding claims~~ claim 1.

26. (currently amended) A host cell containing a nucleic acid molecule according to ~~any one of claims 1 to 24, or a vector according to claim 25~~ claim 1.

27. (canceled)

28. (currently amended) A chimeric receptor protein encoded by a nucleic acid molecule according to ~~any one of claims 18-20~~ claim 18.

29. (canceled)

30. (currently amended) A host cell according to ~~claims 26 or 29~~ claim 26, which is a resting or senescent T-lymphocyte.

31-34. (canceled)

35. (new) A method for treating HIV infection, asthma, eczema, cystic fibrosis, sickle cell anemia, psoriasis, multiple sclerosis, organ transplant rejection, graft-versus-host disease, diabetes, or cancer comprising administering to a patient suffering from such a disease or disorder a therapeutically effective amount of a nucleic acid molecule according to claim 1.



**DOCKET NO.: CELL-0296**

**PATENT**

**Application No.: 10/533,003**

**Preliminary Amendment - First Action Not Yet Received**

36. (new) A method for treating HIV infection, asthma, eczema, cystic fibrosis, sickle cell anemia, psoriasis, multiple sclerosis, organ transplant rejection, graft-versus-host disease, diabetes, or cancer comprising administering to a patient suffering from such a disease or disorder a therapeutically effective amount of a nucleic acid molecule according to claim 18.

37. (new) A composition comprising a nucleic acid molecule according to claim 1 in conjunction with a pharmaceutically acceptable excipient.

DOCKET NO.: CELL-0296  
Application No.: 10/533,003  
Preliminary Amendment - First Action Not Yet Received

PATENT

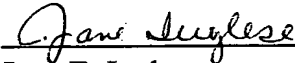
### REMARKS

Following entry of the foregoing amendments, claims 1, 2, 6, 8 to 12, 16 to 19, 21, 25, 26, 28, 30, and 35 to 37 will be pending in the application. Claims 1, 2, 6, 8 to 12, 16 to 19, 21, 25, 26, 28, and 30 have been amended, and claims 3 to 5, 7, 13 to 15, 20, 22 to 24, 27, 29, and 31 to 34 have been canceled, without prejudice, herein to remove improper multiple dependencies, to correct typographical errors, and to place the claims in better form for examination. New claims 35 to 37 have been added. Support for claims 35 to 37 is found throughout the specification as originally filed, including, for example, the original claims. No new matter has been added.

Applicants respectfully submit that the present application is in condition for allowance. Favorable consideration and an early notice of allowance are respectfully requested.

Respectfully Submitted,

Date: October 20, 2005

  
\_\_\_\_\_  
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UNITED STATES PATENT AND TRADEMARK OFFICE

Rec'd PCT/PTO 16 DEC 2005

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www.uspto.gov

U.S. APPLICATION NUMBER NO.

10/533,003

FIRST NAMED APPLICANT

Helene Margaret Finney

ATTY. DOCKET NO.

CELL-0296

INTERNATIONAL APPLICATION NO.

PCT/GB03/04639

I.A. FILING DATE

10/28/2003

PRIORITY DATE

10/30/2002

23377

WOODCOCK WASHBURN LLP  
ONE LIBERTY PLACE, 46TH FLOOR  
1650 MARKET STREET  
PHILADELPHIA, PA 19103

OCT 24 2005

CONFIRMATION NO. 1691

371 FORMALITIES LETTER



\*OC000000017261041\*

Date Mailed: 10/20/2005

### Notification of Insufficient Fees (DO/EO/US)

The following items have been submitted by the applicant or the IB to the United States Patent and Trademark Office as a Designated / Elected Office (37 CFR 1.495).

- Copy of the International Application filed on 04/28/2005
- Copy of the International Search Report filed on 04/28/2005
- Oath or Declaration filed on 04/28/2005
- Request for Immediate Examination filed on 04/28/2005
- U.S. Basic National Fees filed on 04/28/2005
- Priority Documents filed on 04/28/2005

The following items **MUST** be furnished within the period set forth below in order to complete the requirements for acceptance under 35 U.S.C. 371:

- Additional claim fees of **\$3560** as a non-small entity, including any required multiple dependent claim fee, are required. Applicant must submit the additional claim fees or cancel the additional claims for which fees are due.

#### SUMMARY OF FEES DUE:

Total additional fees required for this application is **\$3560** for a Large Entity:

- Total additional claim fee(s) for this application is \$ 3560
  - \$3200 for 64 total claims over 20.
  - \$360 for multiple dependent claim surcharge.

RECEIVED

OCT 24 2005

DOCKET DEPT.  
WWKMN

**ALL OF THE ITEMS SET FORTH ABOVE MUST BE SUBMITTED WITHIN TWO (2) MONTHS FROM THE DATE OF THIS NOTICE OR BY 32 MONTHS FROM THE PRIORITY DATE FOR THE APPLICATION, WHICHEVER IS LATER. FAILURE TO PROPERLY RESPOND WILL RESULT IN ABANDONMENT.**

The time period set above may be extended by filing a petition and fee for extension of time under the provisions of 37 CFR 1.136(a).

Applicant is reminded that any communications to the United States Patent and Trademark Office must be mailed to the address given in the heading and include the U.S. application no. shown above (37 CFR 1.5)

*A copy of this notice **MUST** be returned with the response.*

DARRELL C COTTMAN

Telephone: (703) 308-9140 EXT 203

PART 1 - ATTORNEY/APPLICANT COPY

| U.S. APPLICATION NUMBER NO. | INTERNATIONAL APPLICATION NO. | ATTY. DOCKET NO. |
|-----------------------------|-------------------------------|------------------|
| 10/533,003                  | PCT/GB03/04639                | CELL-0296        |

FORM PCT/DO/EO/923 (371 Formalities Notice)